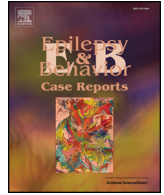




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Case Report

Epilepsy with myoclonic–atonic seizures (Doose syndrome): When video-EEG polygraphy holds the key to syndrome diagnosis



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ABSTRACT

An electroclinical epilepsy syndrome diagnosis enables physicians to predict outcomes as well as select appropriate treatment options. We report a child who presented with reflex myoclonus at the age of 9 months and was initially diagnosed with myoclonic epilepsy in infancy. After 9 years of medically resistant myoclonic seizures, extensive investigations, and emerging learning difficulties, she was referred for video-telemetry to characterize her seizures in an attempt to make a syndromic diagnosis. A three-day video-telemetry assessment was performed to document seizures. Neck and deltoid EMG channels were applied from the onset of the recording.

Frequent generalized bursts of 3- to 5-Hz spike/polyspike and slow wave discharges, associated with clinical manifestations, mostly myoclonic seizures, were noted. In addition, definite atonic components were noted on the neck EMG as well as the deltoids associated with the slow component of the ictal discharges.

The EEG and polygraphy findings are suggestive of a generalized epilepsy characterized by predominantly myoclonic seizures with atonic components. This raises the possibility whether a variant of epilepsy with myoclonic–atonic seizures (Doose syndrome) may be the underlying diagnosis for this girl. A trial of the ketogenic diet would therefore be considered as an option in her future management in view of its beneficial effect in this condition.

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1. Introduction

Classification of the epilepsies into distinct electroclinical epilepsy syndromes has been one of the most significant achievements of modern epileptology. Syndromic diagnosis can provide clinicians with a framework to describe the clinical course, outline prognosis, and make correct therapeutic decisions. Epilepsy syndromes may be identified early in the course of the seizure disorder, sometimes even at the time of initial diagnosis. However, in some cases, the clinical features may not fulfill those required for an established electroclinical epilepsy syndrome, and the epilepsy, therefore, remains undetermined or incompletely classified. In even fewer instances, a fully specified syndrome may be reclassified to another apparently unrelated syndrome in the course of the disease. In these cases, initial information at diagnosis may be difficult to interpret, or the epilepsy syndrome may be in

evolution over time with additional information coming to light to allow more precise later identification.

Here, we report a patient who was initially diagnosed with myoclonic epilepsy in infancy (MEI) at the age of 9 months. Myoclonic seizures were resistant to several antiepileptic drugs (AEDs). In time, cognitive difficulties emerged, and the child was diagnosed with an unclassified form of idiopathic myoclonic epilepsy. Following video-telemetry, additional information regarding seizure semiology proposed the diagnosis of epilepsy with myoclonic–atonic seizures (MAE/Doose syndrome).

2. Case study

A previously healthy girl presented with myoclonic seizures at the age of nine months, initially triggered by unexpected tactile and acoustic stimuli. They were described as sudden and brief generalized jerks involving mostly the neck and upper limb muscles, which sometimes resulted in objects falling from her hands. She had never sustained any injury during these episodes, and they were most often seen when she was tired, unwell, or having a raised temperature. At onset, they were happening once or twice a day, but their frequency gradually

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increased up to 10–15 episodes daily, occurring more spontaneously with time, especially in the early hours of the morning. There was no notable family history and/or any history of febrile seizures.

An electroencephalogram at 21 months revealed generalized polyspike–wave activity both with and without clinical jerks. Her neurological examination and initial development were normal, and she was diagnosed with benign myoclonic epilepsy in infancy (MEI). However, the clinical course of her epilepsy over the following years was neither typical for MEI nor benign.

Initially, she was followed for almost two years without drug treatment. Seizures were brief and self-limiting, and developmental skills were progressing normally. Magnetic resonance imaging brain and baseline investigations were normal. Myoclonic seizures persisted and became more frequent with time. At the age of three years, she was first started on clobazam with minimal therapeutic effect. Following this, she was treated with sodium valproate, topiramate, levetiracetam, and clonazepam without significant benefit. Either her seizures were exacerbated, or she suffered cognitive and behavioral side effects, and as a result, she was weaned off all AEDs since 7.5 years of age. By that time, there were concerns regarding a lack in school progress with problems in math, reading, and working memory. With time, the gap was widening between herself and her peers. She had further metabolic investigations which were normal, including lactate, ammonia, liver functions, organic acids, amino acid, and simultaneous blood and CSF glucose, which excluded a glucose transporter defect. Sequencing of the exons and flanking intron regions of the SLC2A1 gene revealed four well recognized variants that were not considered to be of functional significance. Her EEGs continued to suggest features of a generalized epilepsy, but syndromic classification was still unclear, 8 years after seizure onset.

The child was referred for a three-day video-telemetry at the age of 8.5 years to document seizures. Neck and deltoid EMG channels were

applied at the onset of recording, and on the second day, lower arm and hand EMG channels were also added. During the recording, numerous myoclonic seizures were captured from wakefulness and occasionally from sleep, occurring singly or in brief clusters, associated with generalized bursts of frontally dominant polyspike and wave discharges followed by 3- to 5-Hz slow waves. In several events, some atonic features were also noted, manifesting as isolated head drops or head and arm drops, usually associated with the slow wave component of the discharges (Fig. 1). These occurred in varying combinations, and atonia could precede or follow the myoclonias. The EEG features were suggestive of a generalized epilepsy characterized by predominantly myoclonic seizures with atonic components. In addition, rare absences were also recorded. No bursts of fast polyspikes were evident in sleep, nor were tonic seizures recorded. In cognitive testing, she performed well below average for her age (full-scale IQ of 74) with impaired working memory (WMI 74) and processing speed (PRI 78). Based on these findings, a variant of epilepsy with myoclonic–atonic seizures (MAE/Doose syndrome) was felt possible as the underlying syndromic diagnosis, accounting for the intractability of epileptic seizures as well as for the emerging cognitive difficulties.

3. Discussion

Myoclonic seizures are not characteristic of a specific epilepsy syndrome. There are a wide range of epilepsies in which myoclonic seizures are the most prominent feature ranging from benign self-limiting epilepsies (genetic or familial) to severe progressive myoclonic epilepsies associated with cognitive impairment and unfavorable prognosis. Accurate classification of a patient's syndrome is critical for appropriate management and prognosis. Classification relies on the clinical manifestation of epileptic seizures, EEG findings, age of seizure onset, family history, as well as concomitant neurological manifestations. At times,

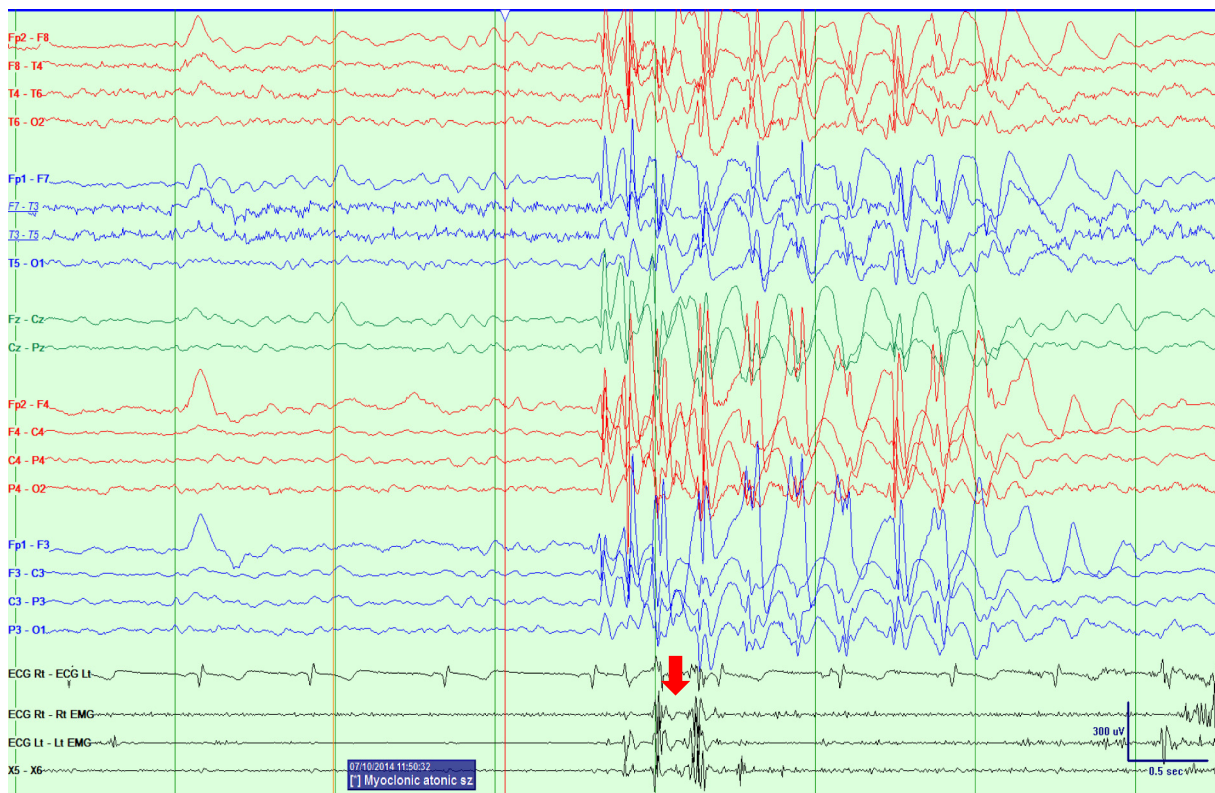


Fig. 1. Ictal EEG with polygraphy of a myoclonic–atonic seizure showing initial myoclonus associated with the burst of polyspikes and atonia on the EMG (arrow) associated with the slow wave component of the discharge (see calibration marker bottom right of figure).

it may be difficult to make a proper syndromic diagnosis at initial presentation as epilepsies may be evolving or may have an atypical presentation. In even fewer instances, a fully specified epilepsy syndrome may be followed in time by another as in the case of a boy described by Auvin and colleagues [1] with myoclonic epilepsy in infancy followed by myoclonic–astatic epilepsy or cases of juvenile myoclonic epilepsy following the diagnosis of MEI described in the literature [1].

Our patient was initially considered to have a diagnosis of benign myoclonic epilepsy in infancy (MEI) which appeared appropriate at the time of seizure onset; however, the subsequent clinical course over the years was not consistent with this condition. The outcome of MEI is generally benign, and seizures are easily controlled with antiepileptic medication, such as sodium valproate, or avoidance of precipitating factors [2,3]. Remission of myoclonic seizures occurs between 6 months to 5 years of onset, but in our patient's case, daily myoclonic seizures proved resistant to four different appropriate antiepileptic drugs. In addition, she developed cognitive problems with concerns regarding lack of academic progress and impaired working memory. Despite a typically favorable neuropsychological outcome seen with MEI, mild cognitive deficits can be observed more frequently than in the general population [3]; however, drug resistance is not a feature consistent with this diagnosis.

Following video-telemetry, a review of the clinical semiology, ictal EEG, and EMG polygraphy revealed the presence of definite atonic features in addition to classical myoclonic seizures suggesting the diagnosis of epilepsy with myoclonic–atonic seizures (MAE/Doose syndrome). Analysis of the ictal EEGs showed that the myoclonic jerks corresponded with the generalized spike/polyspike bursts and the atonia was associated with the slow wave component of the discharge. These findings highlight the importance of polygraphy in aiding accurate EEG interpretation.

The modified ILAE criteria for MAE are [4]: (1) normal development before the onset of epilepsy and absence of organic cerebral abnormalities; (2) onset of myoclonic, myoclonic–astatic, or astatic seizures between 7 months and 6 years of age; (3) presence of generalized spike or polyspike–wave EEG discharges at 2–3 Hz without focal spike discharges; and (4) exclusion of benign myoclonic epilepsy, severe myoclonic epilepsy, and cryptogenic Lennox–Gastaut syndrome based on the ILAE definitions. However, there is no diagnostic test for MAE, and it remains essentially an electroclinical diagnosis.

Our patient fulfills all of the above electroclinical criteria; however, her presentation is not typical of myoclonic–astatic epilepsy; age of seizure onset in our patient is considerably younger than the peak age of 3 to 4 years; nevertheless, one in five children with Doose syndrome can experience their first seizure in the first year of life [4]. Stimulus-elicited (reflex) myoclonic seizures that were prominent at seizure onset are also not a well-known feature of this syndrome. On the other hand, resistance to anticonvulsants and cognitive impairment are present in Doose syndrome with an unfavorable prognosis. The ketogenic diet is the most efficacious treatment option for drug-resistant myoclonic–astatic epilepsy. Following its widely reported success, it has been stated that perhaps it should be considered earlier in the treatment course [5]. In our case, variants of the glucose transporter SLC2A1 gene found in genetic testing may further justify consideration of this option.

In conclusion, our case report emphasizes the difficulty in differentiating the various genetic generalized epilepsies of childhood with myoclonic seizures and highlights the contribution of video-EEG telemetry and EMG polygraphy in appropriately characterizing the seizures and reaching the correct diagnosis. It is especially important to recognize epilepsy with myoclonic–atonic seizures earlier in order to provide the most appropriate management.

Conflict of interest

The authors declare no conflict on interest.

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